

At page 41, line 3 - 13, please delete the paragraph and replace it with the following paragraph:

--Example 2. Evaluation of Triphosphate Analogues

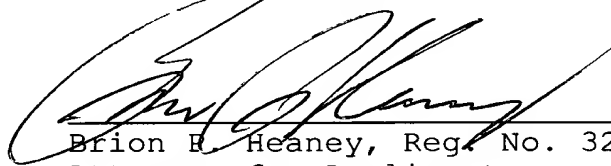
B2 In The HCV RNA-Dependent RNA Polymerase AssayThe following references which are referenced in the example are all incorporated by reference:

1. Behrens, S., Tomei, L., De Francesco, R. (1996) *EMBO* 15, 12-22.
2. Harlow, E, and Lane, D. (1988) *Antibodies: A Laboratory Manual*. Cold Spring Harbord Laboratory. Cold Spring Harbord. NY.
3. Lohmann, V., Körner, F., Herian, U., and Bartenschlager, R. (1997) *J. Virol.* 71, 8416-8428. --

REMARKS

The above-mentioned correct minor obvious typographical errors in the citations of some references at pages 29-32 and 41.

Respectfully submitted,



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VERSION WITH MARKINS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

At page 29, line 3 - page 32, line 27, please delete the paragraph and replace it with the following paragraph:

-- The compounds of the present invention ~~are~~ can be prepared by methods well known in the art. For example, such methods are described in the following references *J. Med. Chem.* **1991**, 34, 693-701; *Chem. Pharm. Bull.* **1995**, 43(11) 2005-2009; *J. Org. Chem.* **1989**, 54, 631-635; *Can. J. Chem.* **1975**, 53(19), 2975-2977; *Nucleosides Nucleotides*, **1990**, 9(8), 1045-60 and *Chemistry of Nucleosides and Nucleotides* edited by Leroy B. Townsend, 1988 Plenum Press Volumes 1 and 2; Synthesis of 2'-- β -fluoro- and 3'- β -fluoro-substituted guanine nucleosides. Effect of sugar conformational shifts on nucleophilic displacement of the 2'-hydroxy and 3'-hydroxy group with DAST. *J. Org. Chem.*, 57(26), (**1992**) 7315-21. Synthesis and antiviral and cytostatic properties of 3'-deoxy-3'-fluoro- and 2'-azido-3'-fluoro-2',3'-dideoxy-D-ribofuranosides of natural heterocyclic bases. *J. Med. Chem.*, 34(7), (**1991**) 2195-2202. Synthesis of 9-(3-deoxy-3-fluoro- β -D-ribofuranosyl)guanine, a new potent antiviral agent. *J. Chem. Soc., Chem. Commun.* (**1989**), (14), 955-7. Synthesis and antiviral activity evaluation of 3'-fluoro-3'-deoxyribonucleosides: broad-spectrum antiviral activity of 3'-fluoro-3'-deoxyadenosine. *Antiviral Res.* (**1989**), 12(3), 133-50. 3'-Fluoro-3'-deoxyribonucleoside 5'-triphosphates: synthesis and use as terminators of RNA biosynthesis. *FEBS Lett.* (**1989**), 250(2), 139-41. Reaction of 1-(2',3'-epoxy- β -D-lyxofuranosyl)uracil with hydrogen fluoride. The unexpected formation of 1-(3'-fluoro-3'-deoxy- β -D-ribofuranosyl)uracil. *J. Heterocycl. Chem.* (1984) ~~(1989)~~, 21(3), 773-5. Synthesis of 3'-

deoxy-3'-fluorouridine. J. Carbohydr., Nucleosides, Nucleotides (1975) ~~(1989)~~, 2(3), 191-5. Synthesis of the 2'-deoxy-2'-fluoro and 3'-deoxy-3'-fluoro analogs of 8-bromoadenosine. Nucleic Acids Symp. Ser. (1997) ~~(1989)~~, 37(Symposium on Nucleic Acids Chemistry, 1997), 17-18. Synthesis of 8-substituted analogs of 3'-deoxy-3'-fluoroadenosine. Nucleosides Nucleotides (1998) ~~(1989)~~, 17(1-3), 115-122. A new synthesis of 3'-fluoro-3'-deoxyadenosine. Nucleosides Nucleotides (1991) ~~(1989)~~, 10(1-3), 719-21. Synthesis of 3'-fluoro-3'-deoxyadenosine starting from adenosine. Synthesis (1990) ~~(1989)~~, (10), 900-5. Synthesis of 3'-deoxy-3'-fluoroadenosine by chemical transglycosidation. Z. Chem. **(1989)**, 29(6), 209-10. Stereoselective synthesis of 3'-deoxy-3'-fluoroadenosine. Bull. Chem. Soc. Jpn. **(1989)**, 62(6), 2119-20. Synthesis of nucleosides fluorinated in the sugar moiety. The application of diethylaminosulfur trifluoride to the synthesis of fluorinated nucleosides. Nucleosides Nucleotides **(1989)**, 8(1), 65-96. Preparation of difluorouridines as antitumor agents. Efficient removal of sugar O-tosyl groups and heterocycle halogens from purine nucleosides with sodium naphthalenide. Tetrahedron (1997) ~~(1989)~~, 53(18), 6295-6302. Synthesis of fluoro and azido derivatives of purine nucleosides from nucleoside 2',3'-cyclic sulfates. Bioorg. Khim. (1994) ~~(1989)~~, 20(11), 1226-30. Synthesis of modified oligomeric 2'-5' A analogs: potential antiviral agents. Helv. Chim. Acta (1991) ~~(1989)~~, 74(1), 7-23. Diethylaminosulfur trifluoride (DAST) as a fluorinating agent of pyrimidine nucleosides having a 2',3'-vicinal diol system. Chem. Pharm. Bull. (1990) ~~(1989)~~, 38(5), 1136-9. Synthesis of 9-(3-deoxy- and 2,3-dideoxy-3-fluoro- β -D-xylofuranosyl)guanines as potential antiviral agents. Tetrahedron Lett. **(1989)**, 30(24), 3171-4. Synthesis and anti-HIV activity of various 2'- and 3'-substituted 2',3'-dideoxyadenosines: a structure-activity analysis. J. Med. Chem. (1987) ~~(1989)~~, 30(11), 2131-7. Adenosine 2',3'-ribo-epoxide.

Synthesis, intramolecular degradation, and transformation into 3'-substituted xylofuranosyl nucleosides and the lyxo-epoxide. J. Org. Chem. ~~(1974)~~(1989), 39(11), 1564-70. Fluoro sugar analogs of arabinosyl- and xylosylcytosines. J. Med. Chem. ~~(1970)~~(1989), 13(2), 269-72. 9-(3-Deoxy-3-fluoro- β -D-xylofuranosyl)adenine and 9-(3-deoxy-3-fluoro- β -D-arabinofuranosyl)adenine. Carbohydr. Res. ~~(1968)~~(1989), 6(3), 347-54. 3',3'-Difluoro-3'-deoxythymidine: comparison of anti-HIV activity to 3'-fluoro-3'-deoxythymidine. J. Med. Chem. ~~(1992)~~(1989), 35(18), 3369-72. Nucleic acid related compounds.

83. Synthesis of 3'-deoxyadenosine-3'-spirocyclopropane, 3'-deoxyuridine-3'-spirocyclopropane, and 5'-deoxy-4',5'-methanoadenosine. Tetrahedron Lett. ~~(1994)~~(1989), 35(21), 3445-8.

8. Synthesis of 2',3'-didehydro-2',3'-dideoxy-3'-C-methyl substituted nucleosides. Nucleosides Nucleotides ~~(1993)~~(1989), 12(8), 865-77. 2',3'-Didehydro-2',3'-dideoxy-2'(and 3')-methyl nucleosides via [3,3]-sigmatropic rearrangements of 2'(and 3')-methylene-3'(and 2')-O-thiocarbonyl derivatives and radical reduction of a 2'-chloro-3'-methylene analog. Can. J. Chem. ~~(1993)~~(1989), 71(2), 186-91. Synthesis and biological activity of 2'(and 3')-deoxy-2'(and 3')-methylenenucleoside analogs that function as mechanism-based inhibitors of S-adenosyl-L-homocysteine hydrolase and/or ribonucleotide reductase. J. Med. Chem. ~~(1992)~~(1989), 35(12), 2283-93.

93. Synthesis and anticancer and antiviral activities of various 2'- and 3'-methylidene-substituted nucleoside analogs and crystal structure of 2'-deoxy-2'-methylidenecytidine hydrochloride. J. Med. Chem. ~~(1991)~~(1989), 34(8), 2607-15.

Stereoselective addition of a Wittig reagent to give a single nucleoside oxaphospetane diastereoisomer. Synthesis of 2'(and 3')-deoxy-2'(and 3')-methyleneuridine (and cytidine) derivatives from uridine ketonucleosides. Synthesis ~~(1991)~~(1989), (4), 282-8. A novel example of unsaturated branched chain sugar nucleoside: 3'-deoxy-3'-

methylenadenosine. *Helv. Chim. Acta* ~~(1981)~~(1989), 64(2), 425-9. Synthesis of 2' (and 3')-deoxy-2' (and 3')-methyleneadenosines and bis(methylene)furan 4',5'-didehydro-5'-deoxy-2' (and 3')-methyleneadenosines. Inhibitors of S-adenosyl-L-homocysteine hydrolase and ribonucleotide reductase. *J. Org. Chem.* ~~(1991)~~(1989), 56(25), 7108-13. Radical and palladium-catalyzed deoxygenation of the allylic alcohol systems in the sugar moiety of pyrimidine nucleosides. *Nucleosides Nucleotides* ~~(1992)~~(1989), 11(2-4), 197-226. Synthesis and NMR spectra of some new carbohydrate modified uridine phosphoramidites. *Nucleosides Nucleotides* ~~(1997)~~(1989), 16(7-9), 1529-1532. New method for the preparation of 3'- and 2'-phosphoramidites of 2'- and 3'-difluoromethylenuridine. *Tetrahedron* ~~(1996)~~(1989), 52(23), 7929-7938. Nucleic acid related compounds. 83. Synthesis of 3'-deoxyadenosine-3'-spirocyclopropane, 3'-deoxyuridine-3'-spirocyclopropane, and 5'-deoxy-4',5'-methanoadenosine. ~~*Tetrahedron Lett.* 1989, 35(21), 3445-8.~~ Some compounds of the present invention are commercially available at Sigma or Aldrich. --

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